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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/127,738	08/03/1998	F. ABEL PONCE DE LEON	002076-005	1682

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/127,738	PONCE DE LEON ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 6-28-04 has been entered.

Claim 24 has been canceled. Claims 1-23 and 25-30 remain pending and are under consideration in the instant office action.

Applicant's arguments filed 6-28-04 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 5, 9, 10, 12, 13, 16-19, 21-23 and 30 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) a method of obtaining avian EG cells comprising: i) isolating PGCs from an avian embryo; and ii) culturing said PGCs in a culture medium comprising LIF, bFGF and IGF, such that avian EG cells are obtained; 2) a method of making a germline chimera to test a population of PGCs for EG cells comprising: i) isolating PGCs from an avian embryo; ii) culturing said PGCs in a culture medium comprising: LIF, bFGF and IGF; iii) transferring said PGCs into a recipient avian embryo; and iv) obtaining a chimeric avian, wherein a germline chimeric avian indicates EG cells were obtained, does not reasonably provide enablement for 1) identifying avian EG cells in a mixed population of avian EG cells and PGCs using mouse stage specific antigen 1, EMA-1 or MC-480, 2) stably transfecting avian EG cells, 3) a method of making germline chimeric avians expressing exogenous

proteins or having a non-wild-type phenotype; or 4) a method of making a somatic cell chimeric avian that is not a germline chimeric avian. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for reasons of record.

Claim 1 is drawn to a method of obtaining EG cells by isolating and culturing PGCs. Claim 9 requires obtaining EG cells that produce mouse-stage specific antigen 1, and/or reacts with EMA-1 or MC-480 antibody. EG cells are equivalent to embryonic stem cells (ES cells), which are defined by their ability to "give rise to all organs of the growing fetus"; this includes germ cells and cells of the placenta (see Pathfinder Encyclopaedia definition of ES cells). Thus, the only way to determine if a cell can give rise to all organs of the growing fetus is to determine if all the organs of chimera's offspring have the ES cell phenotype. As such, claim 9 must result in EG cells capable of making chimeric avians capable of passing the EG phenotype on to its offspring.

Pain of record taught obtaining EG cells from Stage X embryos within a mixed population of PGCs and EG cells that provide germline and somatic cell transmission. Pain taught marker proteins found on the mixed population of cells but did not teach the pattern that distinguishes EG cells from PGCs (pg 2345, col. 2). The specification states EG cells will be identified by their ES antigens or markers, in particular SSEA-1 and 3 marker proteins, and reactivity with EMA-1 and MC-480 antibodies (pg 21, line 16 through pg 22, line 9). The specification taught determining whether PGCs contained EG cells by injecting the PGCs into a recipient blastoderm, producing chimeras, and

determining whether the offspring of the chimeras had the EG cell phenotype (i.e. determining whether the chimeras were germline chimeras; pg 22, lines 15-21; pg 33, line 5; pg 37, line 13).

The specification does not provide adequate guidance that avian EG cells "expressing mouse-stage specific antigen-1 and/or reacts with EMA-1 or MC-480 antibody" as claimed are capable of producing germline chimera avians. The specification does not provide adequate correlation between staining of SSEA-1 and 3 proteins, or reactivity with EMA-1 and MC-480 antibodies and the ability to produce germline and somatic cell chimeras. EMA-1 is not specific to EG cells because it also stains PGCs (pg 22, line 1). While the specification suggests staining patterns for EG cells, EG cells capable of producing germline chimeras were not separated from PGCs and the staining pattern of EG cells capable of producing germline chimeras was not distinguished from that of PGCs. As such, the specification does not enable one of skill to conclude that EG cells capable of producing germline chimeras produce mouse-stage specific antigen 1 or react with EMA-1 or MC-480 antibody as claimed.

Applicants maintain that there is a clear correlation between MC-480 reactivity and avian EG cells in comparison to PGCs. Applicants cite Fig. 6 and 7. Applicants argue that claim 9 merely limits the EG cells obtained to those expressing mouse-stage specific antigen-1 and/or react with EMA-1 or MC-480 (pg 9 of response). Applicants' arguments are not persuasive. The specification as originally filed does not have Fig. 6 or 7. Fig. 1-3 as originally field do not describe PGCs' or EG cells' reactivity with MC-480. Both avian EG cells and PGCs react with MC-480 (pg 42, lines 4-7). The

specification does not teach that cells expressing mouse-specific antigen-1 or that react with EMA-1 or MC-480 are capable of making a germline chimera. Applicants' have not correlated the structure of claim 9 with the function of being able to produce a germline chimera. Applicants have not provided adequate guidance that all cells capable of making germline chimeras express mouse-specific antigen-1 and/or react with EMA-1 or MC-480.

Claim 10 remains rejected because merely transferring the mixed population of cells to a suitable avian embryo is not adequate to determine whether EG cells have been obtained. Transferring the mixed population of cells into an embryo and obtaining somatic cell chimeras that are not germline cell chimeras does not have an enabled use in the instant invention. One of skill can only know that EG cells were present when a germline chimera is obtained.

Applicants argue the rejection is moot because claim 10 has been amended. Applicants' argument is not persuasive. The claim still merely requires transferring the EG cells to a suitable avian embryo without obtaining any offspring, particularly any germline chimeric offspring.

Claim 30 is directed toward making a germline or somatic cell chimeric avian. The claim encompasses making a somatic cell chimeric avian that is not a germline chimeric avian. The specification does not provide an enabled use for making a somatic cell chimeric avian that is not a germline chimeric avian for reasons of record. While making a germline chimeric avian is used to confirm whether a population of

PGCs has EG cells, making a somatic cell chimeric avian does not have a disclosed use in the specification.

Applicants argue somatic cell chimeras have an enabled use for studying development and interactions of genetically different cell types within an individual. Applicants point to pg 13, which states "the expression of an exogenous RNA and/or protein during early embryonic development can be useful for studying tissue-specific and development stage-specific activities of the exogenous RNA or protein." Applicants also state "[i]t was also known in the art at the time that transiently expressed RNA and/or protein could be used to alter the phenotype of an animal by, for example, affecting developmental pathways during embryogenesis." Applicants' arguments are not persuasive. The specification does not describe how to use a somatic cell chimeric chicken to study development, interactions of genetically different cell types, tissue-specific activities of exogenous RNA or protein, or stage-specific activities of exogenous RNA or protein. Studying avian development is a generic use and is not specific to somatic chimeric avians. The specification and the art did not teach why one of skill would study the interactions of genetically different cell types in an avian. The discussion of Naito as it relates to claim 30 is also misplaced because Naito relates to EG cells transfected with a transgene. In conclusion, the specification does not provide adequate guidance for one of skill to use a somatic cell chimeric chicken.

Claims 12, 13, 17-19 and 21-23 remain rejected for reasons of record. Claims 12, 13, 22 and 23 are directed toward a method of obtaining EG cells comprising

transfecting EG cells with a nucleic acid sequence. Claims 17-19 and 21 are directed toward making chimeric avians comprising transferring transfected EG cells into a embryo to make a germline chimeric avian. The only disclosed purpose for transfecting avian EG cells is to make transgenic avians expressing exogenous proteins or having an altered phenotype (pg 7, line 17; pg 2, line 23). Transgenics are defined as organisms having genes from another organism put into their genome (see On-line Medical Dictionary definition provided). EG cells are equivalent to embryonic stem cells (ES cells), which are defined by their ability to "give rise to all organs of the growing fetus"; this includes germ cells and cells of the placenta (see Pathfinder Encyclopaedia definition of ES cells). The specification describes determining if the transgene has been put into the genome of the chimera by determining if the chimera's offspring carry the transgene. While the specification states EG cells may be defined by their structure (i.e. expression of maker proteins, pg 21, lines 16-25), EG cells are defined by their function ability to make germline chimeras (definition provided by Pathfinder Encyclopedia and pg 34, lines 8-13). Applicants have not provided adequate correlative evidence indicating cells expressing mouse-stage specific antigen 1 and/or reacting with EMA-1 or MC-480 are EG cells for reasons cited above. As such, claims 12, 13, 17-19 and 21-23 must result in chimeric avians capable of passing the transfected EG genotype and phenotype on to its offspring.

Naito (March 31 - April 5, 1996, 6th International Symposium on avian endocrinology, "Expression of exogenous DNA in embryonic gonads by transferring primordial germ cells transfected in vitro") isolated PGCs from the blood of a chicken

embryo, transfected the chicken PGCs with a transgene *in vitro,* transferred the PGCs to a recipient chick embryo, obtained a chimeric chicken and obtained expression of the transgene in gonads of the chimeric chicken. Naito did not teach the transfected PGC genotype or phenotype was passed on to its offspring because Naito did not teach making offspring. In fact, Naito (1998, J. Reproduction and Fertility, Vol. 113, pg 137-143) later determined the transgene was lost during embryonic development because it was episomal (see abstract). Therefore, Naito 1996 did not teach how to make germline chimeras using transfected PGCs because the PGCs found in the chimeras' gonads did not have the transgene in their genome.

Allioli of record (1994) taught expressing exogenous DNA in PGCs transfected with a retroviral vector *in vitro*, Allioli did not teach the PGCs were stably transfected or that the PGCs were able to produce chimeric birds expressing exogenous protein or having an altered phenotype.

The art at the time of filing did not teach an ES cell that maintained its ability to become any organ of a developing fetus while maintaining a transgene in its genome. The art at the time of filing did not teach how to make chimeric avians capable of passing the transfected ES cell genotype and phenotype to its offspring; therefore, the art of making such avians was unpredictable. The level of skill in the art was to make a chimeric avian that passed a transgene to its offspring episomally. The specification does not provide any guidance for one of skill to overcome the hurdle described by Naito 1998 so that the transgene would be incorporated into the genome of the EG cell or the offspring of the chimeric chicken. The specification does not teach how to

improve transfection or stability of the transgene in EG cells. Without such guidance it would require those of skill in the art undue experimentation to determine how to make a chimeric avian with gonad cells comprising EG cell comprising a transgene integrated into their genome.

Applicants argue that the combination of the specification, the level of skill in the art and the knowledge available at the time of filing provides an adequate guidance to enable obtaining avian EG cells capable of making germline chimeric avians. Applicants cite Wagner, Naito and Kelder. Applicants' arguments are not persuasive.

The specification teaches transiently transfecting PGCs with DNA encoding marker proteins (1/50 on page 43, line 7, and photographs submitted 5-22-00), but not stably transfecting PGCs (page 20, line 13). The specification does not provide any guidance for one of skill to overcome the hurdle described by Naito 1998 so that stable transfection of the EG cell, incorporation of the transgene into the genome of the EG cell, or passage of the transfected EG cell phenotype to the offspring occurs. Without such guidance it would require one of skill undue experimentation to do so.

Wagner did not teach avian EG cells, transfecting avian EG cells or making germline chimeric avians.

Naito (1996) is discussed above. In addition, Naito is limited to expressing a marker protein encoded by a transgene and does not teach changing the phenotype of the chimeric offspring. It cannot be envisioned how detecting LacZ expression in the gonads of chimeric avians revealed anything about avian endocrinology.

Kelder transfected avian cells but did not teach incorporating a transgene into EG cells or making transgenic avians.

Applicants argue that stable transfection of a cell occurs when the DNA introduced integrates into the genome. Applicants state stable integration of transgenes into cells is well known in the art. Applicants conclude some cells transfected will ultimately be stably transfected (pg 12 of response). Applicants' arguments are not persuasive. The specification teaches transiently transfecting PGCs with DNA encoding marker proteins (1/50 on page 43, line 7, and photographs submitted 5-22-00), but not stably transfecting PGCs (page 20, line 13). Applicants' statement that some cells will ultimately be stably transfected, specifically as it relates to avian ES cells, is unfounded. No one in the art knew of an ES cell that maintained its ability to become any organ of a developing fetus while maintaining a transgene in its genome. In addition, applicants' conclusion is flawed because Naito 1998 taught the transgene introduced into avian EG cells was not stably transfected.

The examiner does not disagree that it may be possible one day to use transfected EG to make a germline chimeric avian; however, the art at the time of filing taken with the guidance provided in the specification would still leave the person of skill in the art with undue experimentation to determine the parameters required to do so.

Applicants argue somatic cell chimeras have a use in the instant application. Applicants argue it was well-known that transiently transfected cells can express an exogenous RNA and/or protein for a significant period of time and be used for many purposes, such as expression of an exogenous RNA and/or protein during early

embryonic development to study tissue-specific and development stage-specific activities of the exogenous RNA or protein. Applicants argue it was also well known that transiently expressed RNA and/or protein could be used to alter the phenotype of an animal by affecting developmental pathways during embryogenesis (¶ bridging pg 12-13 of response). Applicants' arguments are not persuasive. The specification as originally filed did not suggest using somatic cell chimeric avians to study development. The specification as originally filed did not suggest changing the phenotype of somatic cell chimeras. Applicants have not provided any evidence that such uses were well known. For example, Naito 1996 and Naito 1998 did not teach how to use chimeric avians to study development.

Applicants argue somatic cell chimeras were used to study development as evidenced by Naito 1996. "Marking transfected cells with a LacZ transgene as in Naito et al. allow one skilled in the art to track the cell division and migration patterns of marked progenitor cells in a tissue such as the gonad, which provides valuable developmental information" (pg 13 of response). Applicants' argument is not persuasive. The specification does not suggest tracking cell division or migration patterns of marked progenitor cells in tissues of an embryo. Nor does Naito 1996 teach tracking cell division or migration patterns of marked progenitor cells in tissues of an embryo. If injecting transfected avian EG cells into a recipient embryos was used by those of skill in the art at the time of filing to study chicken embryonic development, please point to specific references, include page and line numbers and provide reasoning as necessary.

The specification does not enable transfecting EG cells with DNA encoding a growth factor or enzyme (claims 21 and 23) or isolating an exogenous protein from the egg, systemic circulating system, body fluid or tissue of a chimeric avian (claims 19 and 22). The state of the art at the time of filing was such that the phenotype of transgenic avians with an exogenous transgene was unpredictable (Wall of record, 1996, Theriogenology, Vol. 45, pg 57-68; ¶ bridging pg 61-62). The specification does not provide adequate guidance for one of skill to reasonable predict that the DNA encoding exogenous proteins would be functionally expressed in transgenic avians, where exogenous protein would be expressed in transgenic avians or that the exogenous protein would have a therapeutic effect. Given the unpredictability in the art taken the teachings provided, the specification does not enable transfecting EG cells with DNA encoding a therapeutic protein or determining whether exogenous protein would be expressed in the egg, systemic circulating system, body fluid or tissue of a chimeric avian.

Applicants argue one of skill could easily replace the LacZ gene taught by Naito with a gene encoding a growth factor or any other protein and obtain expression in the chimera or the offspring of the chimera (pg 13, last 13 lines). Applicants' argument is not persuasive. Naito 1996 did not obtain expression of LacZ in the offspring of the chimera, and Naito 1998 taught offspring did not express LacZ. Therefore, it was not well within the ability of those of skill to obtain protein expression. The only purpose for using growth hormones or enzymes is to change the phenotype of the avian as suggested on pg 7, line 17, and pg 2, line 23; Naito 1996, Naito 1998, the specification

and the art as a whole at the time of filing did not suggest expressing growth factors or enzymes as marker proteins like LacZ.

Applicants' argument that "expression could be controlled by means of different tissue-specific promoters" (pg 14, lines 1-2) is unfounded.

Claims 1-23 and 25-30 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

The metes and bounds of what applicants consider PGCs cannot be determined. Applicants previously argued the specification distinguishes avian PGCs from avian EG cells in that avian EG cells stain positive for MC-480 (as well as SSEA-1, SSEA-3 and EMA-1 also found of PGCs) and provide germline and somatic cell transmission upon implantation into recipient embryos while avian PGCs do not stain positive for MC-480 and do not provide somatic cell transmission (pg 21, line 13 through pg 22, line 21). Applicants' argument was not persuasive because PGCs stain positive for MC-480 (pg 42, lines 4-7). It cannot be determined what amount of positive staining distinguishes PGCs and EG cells. Therefore, the metes and bounds of cells that are EG cells within a population of PGCs cultured for a period of time in the presence of LIF, bFGF, SCF and IGF are avian EG cells cannot be determined.

Applicants address this rejection on pg 19 of the response but do not discuss the metes and bounds of PGCs. Applicants state identification of specific EG cells or PGCs would not be required. Applicants' argument is not persuasive because claim 1, step (i),

for example, requires isolating PGCs. It is unclear if a the step is limited to isolating PGCs that become EG cells or if the claim encompasses isolating a population of cells comprising PGCs and EG cells

The rejection of claims 14, 26 and 30 regarding the phrase "cells produced by step (ii) comprising EG cells", has been withdrawn. Claim 14 does not have the phrase. Claims 26 and 30, step ii) now requires maintaining the PGCs for a sufficient time to produce EG cells.

The phrase "said transferred EG cells" in claims 26 and 30 remains indefinite because it lacks antecedent basis. Applicants have not addressed this rejection. Literal support is required when using "said."

Claim Rejections - 35 USC § 102

Claims 1, 4-11, 14-16 and 20 remain rejected under 35 U.S.C. 102(b) as being anticipated by Pain (7-25-96, Development, Vol. 122, pages 2339-2348, UnCover online at http://uncweb.carl.org/uncover/unchome.html) as evidenced by Simkiss (Simkiss, 1994, MacLean, ed., Animals with novel genes, Transgenic birds, Cambridge Univ. Press, Cambridge England, NY, NY, pages 106-137) and under 35 U.S.C. 102(a) as being anticipated by Pain (Aug. 1996, Development, Vol. 122, pages 2239-2348) as evidenced by Simkiss (Simkiss, 1994, MacLean, ed., Animals with novel genes, Transgenic birds, Cambridge Univ. Press, Cambridge England, NY, NY, pages 106-137) for reasons of record.

Pain taught isolating cells from the blastoderm of a stage X chicken embryo, culturing the cells for more than 160 days in the presence of bFGF, IGF, SCF, LIF without feeder cells (pg 2340, col. 1, line 9; pg 2340, col. 1, 4th and 5th full ¶; pg 2345, col. 2, line 10; 2341, col. 2, ¶ 4). The cells expressed EMA-1, SSEA-1 and SSEA-3 for 160 days (pg 243, col. 2, last 2 sentences). Simkiss confirms the cells of Pain included PGCs by teaching stage X chicken embryos contain PGCs (pg 111, Fig. 4.1, top panel). Pain taught introducing the population of cells into stage X chicken embryos and obtaining germline and somatic cell chimeras (pg 2341, col. 1, ¶ 2; pg 2346, col. 2, line 8).

Applicants argue Pain does not teach culturing PGCs as claimed because Pain cultured blastodermal cells from stage X chicken embryos. Applicants' argument is not persuasive. Simkiss confirms the cells of Pain included PGCs by teaching stage X chicken embryos contain PGCs (pg 111, Fig. 4.1, top panel).

Applicants argument that the present invention requires culturing pure isolated PGCs is moot because the claims are not limited to culturing a pure population of PGCs and do not require a step of purifying PGCs from a mixed population.

Applicants argue Pain did not culture cells without feeder cells for more than 160. Applicants' argument is not persuasive. Pain clearly obtained EG cells and showed that undifferentiated avian cells were maintained for 5 days in the absence of feeder cells (pg 2340, col. 1). While Pain taught cells cultured for more than 160 days were obtained using feeder cells (pg 2343, col. 2, 4 lines from the bottom), Pain taught "the cultures" were maintained with or without feeder cells (pg 2341, col. 2, para. 4).

Therefore, Pain taught any of the cultures, including PGCs having EG cells cultured for 160 days (pg 2345), were also cultured without feeder cells.

Claim Rejections - 35 USC § 103

Claims 1, 2, 4-11, 14-16 and 20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Pain (Aug. 1996, Development, Vol. 122, pages 2239-2348) as evidenced by Simkiss (Simkiss, 1994, MacLean, ed., Animals with novel genes, Transgenic birds, Cambridge Univ. Press, Cambridge England, NY, NY, pg 106-137) for reasons of record.

Pain taught isolating cells from the blastoderm of a stage X chicken embryo, culturing the cells for more than 160 days in the presence of 10 ng/ml bFGF, 20 ng/ml IGF, 1% vol/vol SCF, 1% vol/vol LIF without feeder cells (page 2340, col. 1, line 9; page 2340, col. 1, 4th and 5th full paragraphs; page 2345, col. 2, line 10; 2341, col. 2, paragraph 4). The cells expressed EMA-1, SSEA-1 and SSEA-3 for 160 days (page 243, col. 2, last 2 sentences). Simkiss confirms that isolating cells from the blastoderm of stage X chicken embryos of Pain results in isolating some PGCs as claimed by teaching that stage X chicken embryos contain PGCs (page 111, Fig. 4.1, top panel). Pain teaches introducing the cultured PGCs into stage X chicken embryos and obtaining germline and somatic cell chimeras (page 2341, col. 1, paragraph 2; page 2346, col. 2, line 8). The ES cells of Pain are EG cells as claimed because they produce germline and somatic cell chimeric chicks. Obtaining ES cells capable of making germline chimeras as taught by Pain is equivalent to obtaining EG cells (claim

1). Pain does not teach using 0.00625 U/μl LIF, 0.25 pg/μl bFGF, 0.5625 pg/μl IGF, 5.0 pg/μl SCF as in claim 2.

However, Pain taught varying the culture conditions required to obtain EG/ES cells (page 2341, col. 2, "Requirements of specific growth factors and cytokines for CEC and QEC cells"). One of ordinary skill in the art at the time the invention was made would have motivated to use 0.00625 U/μl LIF, 0.25 pg/μl bFGF, 0.5625 pg/μl IGF, 5.0 pg/μl SCF to optimize the conditions required to obtain EG/ES cells.

Applicants describe the teachings of Pain and Simkiss and the deficiencies of Pain and Simkiss but do not describe the deficiencies of Pain and Simkiss when taken together. Applicants' arguments regarding Pain have been addressed above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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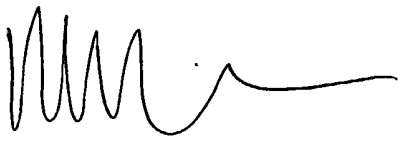
For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER